

## INTERNATIONAL SEARCH REPORT

PCT/G8 02/02668

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12N15/53 C12N9/02

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, INSPEC, SEQUENCE SEARCH

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WILLIAMS PAMELA A ET AL: "Mammalian microsomal cytochrome P450 monooxygenase: Structural adaptations for membrane binding and functional diversity." MOLECULAR CELL., vol. 5, no. 1, January 2000 (2000-01), pages 121-131, XP002222921 ISSN: 1097-2765	14
Y	cited in the application abstract; figure 2; table 1 --- -/--	1-8

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

14 January 2003

Date of mailing of the international search report

27/01/2003

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	VON WACHENFELDT CLAES ET AL: "Microsomal P450 2C3 is expressed as a soluble dimer in Escherichia coli following modifications of its N-terminus." ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, vol. 339, no. 1, 1997, pages 107-114, XP002222918 ISSN: 0003-9861 cited in the application page 109	1-8
Y	COSME JOSE ET AL: "Engineering microsomal cytochrome P450 2C5 to be a soluble, monomeric enzyme. Mutations that alter aggregation, phospholipid dependence of catalysis, and membrane binding." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 275, no. 4, 28 January 2000 (2000-01-28), pages 2545-2553, XP002222919 ISSN: 0021-9258 cited in the application page 2546 -page 2547	1-8
X	HASEMANN C A ET AL: "CRYSTAL STRUCTURE AND REFINEMENT OF CYTOCHROME P450TERP AT 2.3 A RESOLUTION" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 236, no. 4, 1994, pages 1169-1185, XP001120740 ISSN: 0022-2836 cited in the application abstract	14
A	LEWIS DAVID F V: "Homology modelling of human cytochromes P450 involved in xenobiotic metabolism and rationalization of substrate selectivity." EXPERIMENTAL AND TOXICOLOGIC PATHOLOGY, vol. 51, no. 4-5, July 1999 (1999-07), pages 369-374, XP009003755 ISSN: 0940-2993	
A	IBEANU G C ET AL: "IDENTIFICATION OF RESIDUES 99, 220, AND 221 OF HUMAN CYTOCHROME P450 2C19 AS KEY DETERMINANTS OF OMEPRAZOLE HYDROXYLASE ACTIVITY" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 271, no. 21, 24 May 1996 (1996-05-24), pages 12496-12501, XP001017944 ISSN: 0021-9258	

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## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; It is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: in part: 1-11,13,14,18

Purification and crystallizing of cytochrome P450 2C9  
without its structure

2. Claims: 15; in part: 1-14, 18

Purification and crystallizing of P450 2C19 and its structure

3. Claims: 16,19,20; in part: 1-8,10-14,18

Purification and crystallizing of cytochrome P450 2D6  
without its structure; nucleic acid for expression of said  
cytochrome

4. Claims: 17; in part: 1-8,10,11,12,13,14,18

Purification and crystallizing of cytochrome P450 3A4 and  
its structure